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10/656,530

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EXAMINER

LIU, SUE XU

ART UNIT

PAPER NUMBER

1639

NOTIFICATION DATE

DELIVERY MODE

04/14/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No. 10/656,530	Applicant(s) DISTEFANO ET AL.	
	Examiner SUE LIU	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 December 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25-30 and 36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25-30 and 36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/11/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Status

1. Claims 1-24 and 31-35 have been cancelled.
Claims 25-30 and 36 are currently pending.
Claims 25-30 and 36 are being examined in this application.

Election/Restrictions

2. Applicant's election of Group VI (Claims 25-31) without traverse in the reply filed on 10/11/06 is as previously acknowledged.
3. Applicant's election with traverse of the following species in the reply filed on 10/11/06 is as previously acknowledged:
 - A.) Ghrelin receptor as the GH/IGF-1 axis component;
 - B.) A non-human animal model to be contacted by a compound;
 - C.) A small organic molecule as the test compound;
 - D.) A metabolic disorder as a disorder;
 - E.) A cell surface receptor;
 - F.) The species requirement of "A single specific and defined number of nucleotide mutations per nucleic acid sequence" as set forth in the previous Restriction Requirement (mailed 4/11/06, p. 5) is withdrawn.
 - G.) An antagonist;
 - H.) A cell-based assay;

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I.) A human subject as a subject;

J.) The species requirement of “A single selection of an age-associated parameter” as set forth in the previous Restriction Requirement (mailed 4/11/06, p. 5) is withdrawn.

K.) The species requirement of “A single selection of a direct antagonist...” as set forth in the previous Restriction Requirement (mailed 4/11/06, p. 5) is withdrawn.

Priority

4. This application claims priority to the following U.S. Provisional Patent Application Nos. 60/487,308, filed on 7/14/2003, 60/487,344, filed on 07/14/2003, and 60/408,560, filed on 09/06/2002.

Information Disclosure Statement

5. The IDS filed on 7/11/08 has been considered. See the attached PTO 1449 form.

Claim Rejections Maintained

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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(Note: the instant claim numbers are in bold font.)

Smith

7. Claims 25-30 and 36 are rejected under **35 U.S.C. 102(b)** as being anticipated by Smith et al (Endocrine Reviews. Vol. 18(5): 621-645; Oct., 1997; cited previously).

The instant claims recite “A method of identifying a GH/IGF-1 axis antagonist, the method comprising:

a) providing a small molecule that is obtained by chemically modifying an agonist of a GH/IGF-1 axis component selected from the group consisting of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1 R, P I(3) kinase, PDK-1, Akt-1, Akt- 2, or Akt-3 and while retaining a structure of the agonist that is capable of a physical aspect of the interaction of the agonist with the component or that is selected for structural similarity to an agonist of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3;

b) evaluating activity of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3 in vitro, in a cell, or in an organism in the presence of the small molecule, and

c) identifying the small molecule as a GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3 antagonist wherein the small molecule antagonizes the activity of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF- 1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3, thereby providing a GH/IGF-1 axis direct antagonist.

Claim Interpretation: As discussed below, the claim language of the instant claim 25 is unclear and can be interpreted variously. For step a) of the instant claim 25, the claim language appears to dictate various chemical species for the claimed “small molecule”. One interpretation of the claim is that the small molecule can be a “chemically modified” agonist (retaining some structure of the agonist) OR the small molecule can be a chemical that share some “structural similarity” to an agonist. See more discussion below on definitions of an agonist and an antagonist.

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Smith et al, throughout the publication, teach various compounds (peptidomimetics) that can be used for regulation of growth hormone (GH) secretion (see entire document). The reference teaches various compounds (peptides or peptidomimetics) that can modulate activities of at least the GH and GHSR (Ghrelin receptor) in the GH/IGF-1 axis (pp. 621-627; especially, p. 624, right col., p. 625, left col., and p. 630, right col.). The MK-0677 (p. 625, Figure 4), for example, reads on the test compound of the claimed test compound of **clm 25**. The MK-0677 is a derivative of an antagonist or an agonist (p. 624, right col., para 2 and p. 625, left col., para 2), which reads on the chemically modifying an agonist of the GH/IGF-I component of **clm 25**. For example, the reference teaches the MK-0677 compound (which would share structural similarity with the GH agonist) is a derivative generated by modifying GH secretagogues analogs (i.e. GH agonists) such as by chemically modifying the “L-162,725” (a GH releasing enhancing compound) (e.g. p.625, left col.), which read on the product by process recitation of **clm 25**.

The reference also teaches pituitary cell based assay, and GH hormone assay in rats and dogs (p. 625, Left-right col., bridging para), which reads on step b) of **clm 25**, and cell-based assay of **clms 26 and 27**. The reference specifically teaches that the beagles has elevated GH and IGF-I levels after administering MK-0677 (p. 625, left-right col., bridging lines), and thus the beagles has normal IGF-1 levels prior to administering as recited in **clm 28**. The reference's teaching (p. 625, Left-right col., bridging para) also reads on a cohort of adult animals as recited in **clm 29**, and the evaluating step of **clm 31**. The reference teaches administering oral dosage to dogs or rats (p. 625, left col., para 2, p. 635, left-right cols.), which reads on the pharmaceutically acceptable carrier of **clm 36**. The reference also teaches particular dosing regimens of MK-0677 for dogs lowered IGF-I to basal levels (p. 635, right col.) and lowered GH level to basal levels as

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well (p. 636, left col., para 1), which reads on the decreased levels of GH and/or IGF-1 of **clm 30**.

The instant specification defines the term antagonist variously. For example, the instant specification states: “A ‘direct antagonist’ of a particular subject component includes (1) compounds that, at the protein level, directly bind or modify the subject component such that an activity of the subject component is decreased, e.g. by competitive or non-competitive inhibition, destabilization, destruction, clearance, or otherwise...” (spec. p.42, para 3), which definition is broad and encompassing “clearance or destabilization” of the activity levels of the GH/IGF-1 components. Thus, the fact that the MK-0677 lowered IGF-I to basal levels (i.e. destabilizing the increased levels or cleared the increased levels) read on an “antagonist” activity according to the instant specification.

In addition, the instant specification also seems to define the term “antagonist” as acting positively on the GH/IGF-1 components. For example, the instant disclosure states “The agent can be... a direct antagonist, e.g., of a positively acting component of the GH/IGF-1 axis.” (spec., p.5, para 2). That is an antagonist can “positively” act on or activate the GH/IGF-1 components. According to this definition of the instant specification, MK-0677’s ability to increase GH release (i.e. positively acting) also renders the compound an “antagonist” for the GH/IGF-1 components.

Discussion and Answer to Argument

8. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the Smith reference does not teach "direct antagonists". (Reply, p.4).

Applicants state the Smith reference teaches "approximately 120 compounds were selected for their ability to stimulate GH release" and thus these compounds are not antagonists of the GH/IGF-1 axis. However, applicants do not elaborate on reasons why this teaching of the reference would render the compounds not "direct antagonists."

Applicants are respectfully directed to the discussion above for detailed analysis of the Smith reference. The Smith reference teaches administering MK-0677 and observed a decrease or an increase in GH and IGF-1 when using different dosing regimens as discussed above, which properties of the MK-0677 compound renders the compound an antagonist according to the broad definition of the instant specification (see detailed discussion supra).

As discussed above, the instant specification states: "A 'direct antagonist' of a particular subject component includes (1) compounds that, at the protein level, directly bind or modify the subject component such that an activity of the subject component is decreased, e.g. by competitive or non-competitive inhibition, destabilization, destruction, clearance, or otherwise..." (spec. p.42, para 3), which definition is broad and encompassing "clearance or destabilization" of any activity level of the GH/IGF-1 components.

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“During examination, the claims must be interpreted as broadly as their terms reasonably allow. *In re American Academy of Science Tech Center*, 367 F.3d 1359, 1369, 70 USPQ2d 1827, 1834 (Fed. Cir. 2004)” (MPEP 2111.01).

In this case, as discussed supra and previously, the instant specification provides broad definition of the term “antagonist” (or direct antagonist) that encompasses various activity including “decreasing” any activity of the GH/IGF-1 components at any activity level at any time.

As discussed supra, the Smith reference teaches the MK-0677 compound lowered IGF-I to basal levels (i.e. destabilizing the increased levels or cleared the increased levels). That is the said compound, has in fact, “decreased” the IGF-I activity level from a high level to the basal level. Thus, the reference’s teaching read on an “antagonist” activity according to the instant specification’s broad usage of the term “antagonist”.

Applicants also argue the Smith reference does not teach the recitation of “while retaining a structure of the agonist...” (Reply, pp.4-5).

Applicants are respectfully directed to the above discussion as well as the discussion below under 35 USC 112, 2nd paragraph. It is also noted, the said recitation is only one alternative embodiment of the instant claim 25 (as the said claim can be interpreted variously). The Smith reference teaches compounds sharing similar structures with various known agonists of the GH/IGF-1 components as discussed supra, and thus the said compounds read on the “small molecules” of the instant claims.

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Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Blum

11. Claims 25, 26 and 36 are rejected under **35 U.S.C. 102(b)** as being anticipated by or, in the alternative, under **35 U.S.C. 103(a)** as obvious over Blum et al (Biochemistry. Vol. 39: 15705-15712; 2000; cited in IDS).

Blum et al, throughout the publication, teach using inhibitors to inhibit IGF-1 receptor (Abstract). The reference teaches using various inhibitors such as I-OMe AG 538 for inhibition of IGF-1R (e.g. p.15707, right col. para 6; Table 1), and chemical synthesis of the inhibitor (e.g. p.15706, col.1, para 3), which read on step a) of **clm 25**. Although the reference does not explicitly teach the inhibitors are “obtained by chemically modifying an agonist” or “is selected for structural similarity to an agonist” as recited in **clm 25**, the phrase “obtained by chemically modifying an agonist” or “is selected for structural similarity to an agonist” is a recitation of product-by-process limitation.

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“[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith.” In re Brown, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Process steps *per se* cannot serve to limit the product claims. See In re Stephens, 345 F.2d 1020, 1023, 145 USPQ 656, 658 (CCPA 1965) (“We think it well settled that the presence of process limitations in product claims, which product does not otherwise patentably distinguish over the prior art, cannot impart patentability to that product.”). The relevant inquiry in a product-by-process claim is how the process recitations might define structure. See, e.g., In re Garner, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1969) (recitation of “interbonded one to another by interfusion between the surfaces of the perlite particles” construed as structural limitation in product claim); In re Dike, 394 F.2d 584, 589, 157 USPQ 581, 585 (CCPA 1968) (no error in USPTO board holding that term “blowmolded” in claims drawn to integral plastic container and handle failed to distinguish over prior art, because term related to process of making the article, and was not definitive as to the structure of the article). Here, the process step “obtained by chemically modifying an agonist” does not add a structural limitation to the “small molecule” (or the “antagonist”) because the resulting compounds would have the same structure. The Blum reference teaches syntheses of I-OMe AG 538 and AG 538 (e.g. p.15706; p.15708), which compounds can be chemically modified natural ligands of the IGF-1 receptor kinase. The instant specification recites that an antagonist can be compounds that are analogs or modification of the natural occurring ligands (or substrates) of cell receptors, and “kinase

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inhibitors” are antagonists (see Spec. PGPUB version, [0116]). According to the instant specification, the “kinase inhibitors” of the Blum reference are structurally the same as the compounds encompassed by the term “antagonists” as it is used in the instant specification. Thus, this process limitation does not impart patentability to the claimed “small molecule” in accordance with *In re Dike*.

In addition, the IGF-1 receptor kinase inhibitors of the Blum reference are structurally similar to the substrate (or ligand, or an agonist) of the IGF-1 receptor kinase (i.e. a tyrosine residue), and thus would be a chemical modification of the compound, tyrosine, or an agonist.

The reference also teaches incubating the inhibitors with cells for testing the inhibitors abilities to inhibit (or antagonize) IGF-1R in both cell and cell free systems (e.g. p.15709; p.15706), which read on step b) and c) of **clm 25** and **clm 26**.

The reference also teaches using various buffers or solutions for incubation of the inhibitors with cells (e.g. p.15706, col.2, para 2 and 4), which the solutions and buffers read on pharmaceutically acceptable carrier of **clm 36**.

Discussion and Answer to Argument

12. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the cited reference does not teach all elements, specifically, “an agonist” (Reply, p.8).

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Applicants are respectfully directed to the above discussion on how the cited reference teaches all element of the claimed invention. As discussed above, the phrase “obtained by chemically modifying an agonist” is a product-by-process limitation.

Here, the process step "obtained by chemically modifying an agonist... while retaining a structure..." does not add a structural limitation to the “small molecule” (or the “antagonist”) because the resulting compounds would have the same structure. The Blum reference teaches syntheses of I-OMe AG 538 and AG 538 (e.g. p.15706; p.15708), which compounds can be chemically modified natural ligands of the IGF-1 receptor kinase. The instant specification recites that an antagonist can be compounds that are analogs or modification of the natural occurring ligands (or substrates) of cell receptors, and “kinase inhibitors” are antagonists (see Spec. PG PUB version, [0116]). According to the instant specification, the “kinase inhibitors” of the Blum reference are structurally the same as the compounds encompassed by the term “antagonists” as it is used in the instant specification. These kinase inhibitors compete with the natural substrate of the receptor kinase and are also structurally similar to the natural ligand, and thus, these inhibitors are structurally similar to the an agonist. Therefore, this process limitation does not impart patentability to the claimed “small molecule” in accordance with *In re Dike*.

In addition, Applicants’ assertion of the “substrate” of one of the IGF-1 component is NOT an agonist is in direct conflict with the explicit broad definition provided in the instant specification. The instant specification states “A ‘direct agonist’ of a particular subject component includes (1) compounds that, at the protein level, directly bind or modify the subject component such that an activity of the subject component is increased, e.g., by activation, stabilization...” (spec. p.43). The substrate of the kinase of the Blum reference would “activate”

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the kinase as explicitly taught by the reference (“Upon ligand [substrate] binding...activation of the receptor” (Blum, p.15705)).

Orrego

13. Claims 25-30 and 36 are rejected under **35 U.S.C. 102(a)** as being anticipated by or, in the alternative, under **35 U.S.C. 103(a)** as obvious over Orrego et al (Journal of Clinical Endocrinology and Metabolism. Vol. 86(11): 5485-5490; cited in IDS).

Orrego et al, throughout the publication, teach using an antagonist of GHRH-R to reduce GH in human (Abstract). The reference teaches administering a GHRH antagonist to human such as (N-Ac-Tyr1, D-Arg2)GHRH-(1-29)-NH2) or GH-44, which compounds are modification of the GHRH (an “agonist”) or is “structurally similar to an agonist” of the GH/IGF-1 axis components listed in **clm 25**. (e.g. p.5486, col.1, para 1; Figure 1; Figures 2-4). The GHRH antagonists read on the antagonist obtained from an agonist of **clm 25**, and the administering reads on the steps of **clm 25**. Although the reference does not explicitly teach the inhibitors are “obtained by chemically modifying an agonist” or “is selected for structural similarity to an agonist” as recited in **clm 25**, the phrase “obtained by chemically modifying an agonist” or “is selected for structural similarity to an agonist” is a recitation of product-by-process limitation.

“[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before

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it and then obtain prior art products and make physical comparisons therewith.” In re Brown, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Process steps *per se* cannot serve to limit the product claims. See In re Stephens, 345 F.2d 1020, 1023, 145 USPQ 656, 658 (CCPA 1965) (“We think it well settled that the presence of process limitations in product claims, which product does not otherwise patentably distinguish over the prior art, cannot impart patentability to that product.”). The relevant inquiry in a product-by-process claim is how the process recitations might define structure. See, e.g., In re Garnero, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1969) (recitation of “interbonded one to another by interfusion between the surfaces of the perlite particles” construed as structural limitation in product claim); In re Dike, 394 F.2d 584, 589, 157 USPQ 581, 585 (CCPA 1968) (no error in USPTO board holding that term “blowmolded” in claims drawn to integral plastic container and handle failed to distinguish over prior art, because term related to process of making the article, and was not definitive as to the structure of the article). Here, the process step “obtained by chemically modifying an agonist” does not add a structural limitation to the “small molecule” (or the “antagonist”) because the resulting compounds would have the same structure. The Orrego reference teaches using (N-Ac-Tyr1, D-Arg2) peptide (e.g. p.5486), which compounds can be chemically modified natural ligands of the GHRH-R. The instant specification states “N-acetyl-Tyr1, D-Arg2” is an example of GHRH antagonists, and is also a modified version of the GHRH agonist (see Spec., PG PUB version, para [02311]+). Thus, at least the antagonist (or N-Ac-Tyr1, D-Arg2) of the reference is “structurally similar” to an agonist of GHRH-R. In addition, it is also a modification of the GHRH-R agonist according to the instant specification. Thus, the peptide of the reference is structurally the same as the claimed “small molecule” of the instant claims.

The reference also teaches various assays for measuring GH levels (e.g. p.5486, left col., para 3), which reads on steps b and c of **clm 25** and the cell free assay of **clm 26**.

The reference teaches administering the compounds to adult humans (e.g. Table 1), which reads on the limitation of **clm 27**.

The reference also teaches the adult humans have normal IGF-1 levels (e.g. Table 2; p. 5485, right col.), which reads on the limitations of **clms 28, 29** and **30**.

The reference also teaches administering the antagonists as boluses (e.g. Figure 1; p.5486, left col., para 1), which read on the pharmaceutical carrier of **clm 36**.

Discussion and Answer to Argument

14. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants seem argue the cited reference does not teach all elements (Reply, p.7).

However, applicants do not elaborate on which specific elements were missing from the cited reference. Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

Applicants are respectfully directed to the above discussion on how the cited reference teaches all element of the claimed invention. As discussed above, the peptide of the reference is structurally similar to an agonist of GHRH-R, as well as a modification of GHRH (an agonist of

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GHRH-R). Thus, the peptide used in the cited reference is structurally the same as the instant claimed inventions.

Applicants continue to assert Orrego “fails to disclose evaluating activity of a GH/IGF-1 activator in the presence of a small molecule...” (Reply, p.7).

As discussed above and previously, the reference teaches evaluating the activity of the GH/IGF-1 components such as evaluating the activity of the GH level (e.g. p.5486, left col., para 3). The reference also teaches using the identified peptide , N-Ac-Tyr1, D-Arg2, to decrease GH levels, and thus identifying the peptide as an antagonist (e.g. p.5486, para 1).

New Claim Objection(s) / Rejection(s)

Claim Rejections - 35 USC § 112

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter Rejection

16. Claim 25-30 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is necessitated by applicant’s amendments to the claims.

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Claim 25 has been amended to recite “while retaining a structure of the agonist that is capable of a physical aspect of the interaction of the agonist with the component” as filed on 12/5/08. However, the instant specification does not provide support for the claimed recitation of “retaining a structure of the agonist that is capable of a physical aspect of the interaction of the agonist with component”.

Applicants have pointed to page 42 (second full paragraph) for support. However, the said passage in the instant specification only provides a broad description for the term “activity of the GH/IGF-1 axis”. There is no description regarding the above said claim language.

Applicants also point to page 54, first paragraph for support. The passage of the instant specification only recites “Modification or similarity to the agonist may retain some physical aspects of the interaction...” The said passage of the instant specification does not provide support for “retaining a structure of the agonist” in its full scope.

If Applicant believes this rejection is in error, applicant must disclose where in the specification support for the entire scope of the amendment(s) and/or new claims can be found. As a result, Claim 25 and its dependent claims represent new matter.

Second paragraph of 35 U.S.C. 112

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 25-30 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

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applicant regards as the invention. This rejection is necessitated by applicant's amendments to the claims.

Claim 25 has been newly amended to recite "while retaining a structure of the agonist that is capable of a physical aspect of the interaction of the agonist with the component", which recitation is unclear and renders the said claim indefinite. First, it is not clear what the said recitation is modifying. It is not clear if the said recitation is modifying the method step of "providing a small molecule" or if the said recitation is modifying the product-by-process recitation of "obtained by chemically modifying an agonist."

In addition, the phrase "is capable of a physical aspect of the interaction" is confusing and unclear. The instant specification does not provide a specific definition for the term "physical aspect of the interaction". It is not clear what the said phrase is referring. Further, the recitation "a structure... that is capable of a physical aspect of the interaction" is also not specifically defined in the instant specification. It is not clear to which structure the phrase is referring and to what (action) the said structure is "capable" of.

Further, the instant claim 25 also recites "or that is selected from structural similarity..." after the said recitation of "while retaining". It is not clear what the term "that" is referring. It is also not clear whether or not the choices of "small molecule" include the "structural similarity to an agonist." In other words, the instant claim 25 appears to be written in an improper Markush format. It is not clear what chemical species are encompassed by the genus of "small molecule".

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Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sue Liu/
Primary Examiner, AU 1639
4/9/09

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